

16: Enroth et al., Occurrence of resistance mutation and clonal expansion in *Helicobacter pylori* multiple-strain infection: a potential risk in clarithromycin-based therapy. Clin Infect Dis. 1999 Jun; 28(6):1305-7.

17: Hua et al., Predominance of a single strain of *Helicobacter pylori* in gastric antrum. Helicobacter. 1999 Mar; 4(1):28-32.

18: van Doorn et al., *Helicobacter pylori*-associated gastritis in mice is host and strain specific. Infect Immun. 1999 Jun; 67(6):3040-6.

19: van Doorn et al., The inflammatory response in CD1 mice shortly after infection with a CagA+/VacA+ *Helicobacter pylori* strain. Clin Exp Immunol. 1999 Mar;115(3):421-7.

20: De Ungria et al., Molecular characterization and interstrain variability of pHPS1, a plasmid isolated from the Sydney strain (SS1) of *Helicobacter pylori*. Plasmid. 1999 Mar; 41(2):97-109.

In treating or preventing a disease or disorder caused by *H. pylori* infection, the compounds of the present invention can be used alone or can be used in combination with an anti-*H. pylori* agent. Any suitable anti-*H. pylori* agent can be used in combination with the compounds of the present invention. Such exemplary anti-*H. pylori* agents include proton-pump inhibitor (PPI), metronidazole, clarithromycin, amoxicillin and famotidine (Gaschwantler et al., *Eur. J. Gastroenterol Hepatol.*, 10(7):579-82 (1998)).

In a preferred embodiment, the compounds of the present invention are used without administering an anti-*H. pylori* agent such as PPI, metronidazole, clarithromycin, amoxicillin and famotidine. More preferably, the compounds of the present invention are used to treat or prevent diseases or disorders caused by a *H. pylori* resistant strain induced by PPI, metronidazole, clarithromycin amoxicillin or famotidine treatment.

The compounds of the present invention, alone or in combination with other suitable anti-*H. pylori* agents, can be administered by any suitable methods. For example, the compound or a pharmaceutically acceptable salt thereof of the present invention can be administered by intracavernous injection, subcutaneous injection, intravenous injection, intramuscular injection, intradermal injection, oral administration, or topical administration.

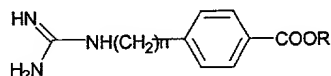
In a specific embodiment, the present method further comprises a step of diagnosing or pragnosing *H. pylori* infection in the subject. Any suitable method for

diagnosing or pragnosing *H. pylori* infection can be used. The prognosis or diagnosis can be based upon the detection and/or identification of any or all *H. pylori* protein(s) such as its enzymes, antigens and antibodies, nucleic acid(s), or other pathological or clinical markers and symptoms. For example, the diagnosing or pragnosing methods disclosed in WO 01/44815 and U.S. Patent No. 5,571,674 can be used.

D. Combinations, kits and combinatorial methods

In still another aspect, the present invention is directed to a combination, which combination comprises an agent that selectively inhibits DNA replication initiation in *E. coli* or *H. pylori*, or a pharmaceutically acceptable salt thereof, and an anti-*H. pylori* or anti-*E. coli* agent.

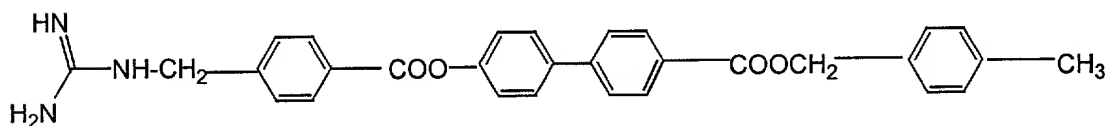
Preferably, the combination comprises a compound, or a pharmaceutically acceptable salt thereof, having the following formula II:



wherein n is an integer from 0-1, and R is elected from the group consisting of hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ aryl and



and an anti-*H. pylori* agent. More preferably, the compound to be included in the combination has the following formula III (Ne-2001):



Any suitable anti-*H. pylori* agent can be used in the present combination. In a specific embodiment, the anti-*H. pylori* agent used in the combination is PPI, metronidazole, clarithromycin, amoxicillin or famotidine.

In another specific embodiment, a method for treating or preventing a disease or disorder caused by bacterial infection, e.g., *E. coli* or *H. pylori* infection, is provided,

which method comprises administering, to a subject to which such treatment or prevention is needed or desirable, an effective amount of the above combination, or a pharmaceutically acceptable salt thereof, thereby said disease or disorder is treated or prevented.

5 In yet another specific embodiment, a kit is provided, which kit comprises the compound of the present invention, or a pharmaceutically acceptable salt thereof, and an instruction for using said compound or pharmaceutically acceptable salt in treating or preventing a disease or disorder caused by a bacterial infection, *e.g.*, *E. coli* or *H. pylori* infection.

10 In yet specific embodiment, a kit is provided, which kit comprises the above combination, and an instruction for using said combination in treating or preventing a disease or disorder caused by a bacterial infection, *e.g.*, *E. coli* or *H. pylori* infection.

E. Formulations and dosages

15 According to the present invention, the compounds of the present invention, alone or in combination with other agents, carriers or excipients, may be formulated for any suitable administration route, such as intracavernous injection, subcutaneous injection, intravenous injection, intramuscular injection, intradermal injection, oral or topical administration. The method may employ formulations for injectable administration in unit dosage form, in ampoules or in multidose containers, with an added preservative. 20 The formulations may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, sterile pyrogen-free water or other solvents, before use. Topical administration in the present invention may employ the use of a foam, gel, 25 cream, ointment, transdermal patch, or paste.

Pharmaceutically acceptable compositions and methods for their administration that may be employ for use in this invention include, but are not limited to those described in U.S. Patent Nos. 5,736,154; 6,197,801 B1; 5,741,511; 5,886,039; 5,941,868; 30 6,258,374 B1; and 5,686,102.

The magnitude of a therapeutic dose in the treatment or prevention will vary with the severity of the condition to be treated and the route of administration. The dose, and